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1: *Lab Invest.* 1998 Aug;78(8):967-72.

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**Antisense oligonucleotides against collagen-binding stress protein HSP47 suppress collagen accumulation in experimental glomerulonephritis.**

**Sunamoto M, Kuze K, Tsuji H, Ohishi N, Yagi K, Nagata K, Kita T, Doi T.**

Department of Clinical Bio-Regulatory Science, Faculty of Medicine, Kyoto University, Japan.

Heat shock protein 47 (HSP47) is a collagen-specific molecular chaperone that has been shown to play a major role during the biosynthesis and secretion of procollagen molecules. The expression of HSP47 has been reported to increase in parallel with the expression of collagens during the progression of various fibrosis models. However, it remains unclear whether an inhibition of HSP47 overexpression would suppress collagen accumulation and thus reduce the progression of fibrotic diseases. In this study, we attempted to attenuate glomerular collagen accumulation by inhibiting the overexpression of HSP47 with antisense oligodeoxynucleotides in an experimental glomerulonephritis model induced by anti-Thy-1 antibodies. The administration of antisense oligodeoxynucleotides against HSP47 at the induction of the glomerular disease markedly suppressed the increased production of collagens and attenuated the histologic manifestations of the disease. These results provide direct evidence of a pivotal role for HSP47 in the pathogenesis of glomerulonephritis.

PMID: 9714184 [PubMed - indexed for MEDLINE]

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1: Kidney Int Suppl. 1997 Dec;63:S232-5.

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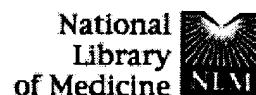
## TCV-116 inhibits interstitial fibrosis and HSP47 mRNA in rat obstructive nephropathy.

**Moriyama T, Kawada N, Akagi Y, Ando A, Horio M, Yamauchi A, Nagata K, Imai E, Hori M.**

First Department of Medicine, Osaka University School of Medicine, Faculty of Health, Japan. [toshiki@medone.med.osaka-u.ac.jp](mailto:toshiki@medone.med.osaka-u.ac.jp)

Unilateral ureteral obstruction (UUO) is a well established disease model leading to fibrosis of the obstructed kidney. In this model, involvement of enhanced renin-angiotensin system in the pathogenesis of interstitial fibrosis has been demonstrated. A 47-kDa heat-shock protein (HSP47) was originally identified as a collagen-binding stress protein, and is currently considered to be a collagen-specific molecular chaperone that plays a pivotal role during the biosynthesis and secretion of procollagen from endoplasmic reticulum. To test if HSP47 is involved in interstitial fibrosis in UUO, we examined the expression of HSP47 mRNA in rat UUO kidneys after 12 hours, 1, 4, 7 days of obstruction. HSP47 mRNA expression was significantly increased as early as 12 hours after obstruction and was sustained at the increased level until seven days. Type I collagen mRNA significantly increased after four days of UUO. Fibrotic changes of interstitium appeared in Masson's trichrome stained section after four days. To explore the possible involvement of angiotensin II (Ang II) in HSP47 induction, the effect of Ang II receptor antagonist (TCV-116) and angiotensin converting enzyme inhibitor (lisinopril) was tested. TCV-116 or lisinopril was given to the animals orally once a day at the dose of 10 mg/kg. TCV-116 or lisinopril significantly ameliorated the fibrotic change of interstitium seven days after obstruction. HSP47 and type I collagen mRNA levels in the TCV-116- or lisinopril-treated groups were reduced to about 60% of untreated UUO. A possible involvement of HSP47 in the pathogenesis of interstitial fibrosis in UUO is suggested; however, further investigation is required to identify the signals involved in the induction of HSP47 in UUO.

PMID: 9407468 [PubMed - indexed for MEDLINE]



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